UNITED STATES DEPARTMENT OF COMMERCE
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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.
09/482,682	01/14/00	VON SEGGERN	D 1294.0010001

HM22/0620
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EXAMINER
FOLEY,S

ART UNIT	PAPER NUMBER
1648	

DATE MAILED: 06/20/01

Please find below and/or attached an Office communication concerning this application or proceeding.

Commissioner of Patents and Trademarks

Office Action Summary	Application No.	Applicant(s)	
	09/482,682	VON SEGGERN ET AL.	
	Examiner	Art Unit	
	Shanon A. Foley	1648	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136 (a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☐ Responsive to communication(s) filed on _____ .

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) 1-94 is/are pending in the application.

4a) Of the above claim(s) 24-40,42-46,48-68 and 71-94 is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) 1-23,41,47,69 and 70 is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claims _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are objected to by the Examiner.

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. § 119

13)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☒ Acknowledgement is made of a claim for domestic priority under 35 U.S.C. § 119(e).

Attachment(s)

15)☒ Notice of References Cited (PTO-892)
16)☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
17)☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s) _____ .
18)☐ Interview Summary (PTO-413) Paper No(s). _____ .
19)☐ Notice of Informal Patent Application (PTO-152)
20)☐ Other: .

DETAILED ACTION

Election Restriction

Applicant's election with traverse of Group I in Paper No. 7 is acknowledged. The traversal is on the ground(s) that there is not a search burden to examine all groups I-VI because the search for art for any of the groups would also result in information about other adenovirus particles. As an example, applicant argues groups II-V are classified in the same class. Applicant argues that groups II and III should also be rejoined because the search for fiber-altered adenovirus would turn up fiber-less adenovirus. Applicant also states that art pertaining to adenovirus particles would result in art for making the product.

This is not found persuasive because each of the adenovirus particles claimed have independent and distinct features, which must be considered separately for patentability. As applicant pointed out, some of the particles share the same class. Applicant should note that none of the particles share identical subclasses due to the unique features claimed for each particle. A search in three entire classes and six entirely different subclasses in patent literature would constitute a burdensome search in and of itself. This does not preclude a worldwide non-patent literature search for each patentably distinct invention. Therefore, examination of more than one invention would involve undue burden. In response to the arguments regarding searching a product would find art on how to make the product, unique products sometimes require unconventional methods of making the product, therefore, the method of making the product is patentable subject matter. In summary, claims 24-40, 42-46, 48-68, 71-94 are withdrawn from consideration due to the non-election of inventions of groups II-VI and claims 1-23, 41, 47, 69, and 70 of group I are under consideration.

The requirement is still deemed proper and is therefore made FINAL.

Claim Rejections - 35 USC § 112

Claim 1-23, 41, 47, 69, and 70 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claim 1 is drawn to a tripartite leader (TPL) sequence encodes first, second, or third, different TPL exons. It is unclear what is meant to be different about the exons. Are the exons derived from TPL exons from different adenoviruses?

Claim 4 recites the limitation "intron" in lines 1 and 2. There is insufficient antecedent basis for this limitation in the claim.

Claim 6 recites the limitation "promoter" in line 3. There is insufficient antecedent basis for this limitation in the claim.

Claim 11 is recites a "vector complementing plasmid". It is unclear what this is. Is the vector sequence a compliment of the sequence in the plasmid?

Claim 17 recites the limitation "chimeric" in line 1. There is insufficient antecedent basis for this limitation in the claim.

Claim 22 states that the cell line produces one protein, which is denoted as "an" adenovirus protein, but further states that the cell line produces an adenovirus early gene and a fiber gene (emphasis added). Claim 21 indicated that the cell line supports the production of a viral gene, not genes, which is indicated in the second portion of claim 22. Claim 22 further indicates that the cell line produces these genes in order to complement the genes that are deficient in the vector genome. However, none of the preceding claims (1-20) indicated that the

vector genome was deficient in any way. For example, claim 17 is drawn to an adenovirus that "comprises" an Ad3 head domain and an Ad5 tail domain. The claim does not suggest that the adenovirus is missing parts. Therefore, the claims are vague and confusing as to what the adenovirus vector genome actually comprises.

Claim 23 is vague and indefinite because the claim is stating that a singular deficient gene is complemented by the expression of the gene under an inducible promoter and is dependent from claim 22. Are both the early and the fiber gene under the control of the inducible promoter, or is only one gene under control of that particular kind of promoter?

Claim 41 recites the phrase "alternatively operatively linked" to a promoter. It is unclear what the relationship is of the gene and the promoter.

Claims 41 and 47 are vague and indefinite for depending from claims in a non-elected group. To expedite prosecution, claim 41 is considered as dependent from claim 21 and claim 47 is considered to be dependent from 1. However, applicant is required to amend the claim to correct dependency.

Claim 69 recites the limitation "packaging cell line" in line 1. There is insufficient antecedent basis for this limitation in the claim. The claim is dependent from claim 12, which is drawn to a nucleic acid. In the interest of compact prosecution, the claim will be considered to depend from claim 20. However, applicant is required to amend the claim to correct dependency. Claim 69 is also unclear because the packaging cell line is selected from specific cell lines and an epithelial cell line (emphasis added). Are there two cell lines that are mixed together somehow to form a conglomerate cell line? If "or" is intended in lieu of and, does this mean that

that if one chose the other cell lines in the list, such as 293 cells, that cell line does not require the stably integrated nucleic acid molecule, as required by the epithelial cell line?

Claim 70 recites the limitation "particle" in line 1. There is insufficient antecedent basis for this limitation in the claim. The claim is dependent from claim 21, which is drawn to a cell line supporting the production of an adenovirus vector genome and does not mention particles. Claim 70 recites the limitation "exogenous protein" in line 2. There is insufficient antecedent basis for this limitation in the claim. As noted before, the claim is dependent on claim 21, which does not recite an exogenous protein. In addition, claim 21 indicates that the adenovirus vector is supported by complementation of a deficient viral gene. The deficient gene of claim 21 is understood to be required by the recombinant in order to get propagation. Claim 70 states that an exogenous gene is a tumor-suppressive gene or a suicide protein. Adenoviruses do not require either gene for propagation. Therefore, it is unclear what applicant intends by "exogenous protein". The claim is further vague and indefinite because it cannot be determined what the structural and functional metes and bounds of what a "biologically active fragment" of a tumor-suppressive gene and/or a suicide protein are.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (a) the invention was known or used by others in this country, or patented or described in a printed publication in this or a foreign country, before the invention thereof by the applicant for a patent.
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claims 1-4, 6, 7, 9-16, 20-23, 41, 47, and 69 are rejected under 35 U.S.C. 102(a) as being clearly anticipated by Memerow et al. in WO 98/13499.

The claims are drawn to a nucleic acid comprising an adenovirus tripartite leader sequence that comprise a partial first, second, or third TPL exons that are operatively linked and further encodes an adenovirus fiber protein, which is expressed in plasmid pCLF. The claims are further drawn to a epithelial packaging cell line that that has stably integrated the said nucleic acid, which is SEQ ID NO: 26 under the control of an inducible promoter. The recombinant adenovirus particle produced by the cell line contains a tumor suppressor protein. The teachings of Memerow et al. anticipate these claims 1-4, 6, 7, 9-16, 20-23, 41, 47, and 69. See the abstract, claims 1-50, and the sequence alignment of SEQ ID: 26 in the instant application in comparison with SEQ ID: A59054 provided with the filing of WO 98/13499.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

Claims 8 and 17 are rejected under 35 U.S.C. 103(a) as being unpatentable over Memerow et al. as applied to claims 1-4, 6, 7, 9-16, 20-23, 41, 47, and 69 above, and further in view of Stevenson et al.

See the teachings of Memerow et al. above. Memerow et al does not teach a recombinant adenovirus nucleic acid comprising a chimeric head and tail domain from Ad3 and Ad5. However, Stevenson et al. does, see the abstract. One of ordinary skill in the art at the time the

invention was made would have been motivated to incorporate a chimeric adenovirus Ad3 fiber head domain fused with an Ad5 fiber tail domain taught by Stevenson et al. with the adenovirus nucleic acid molecule taught by Memerow et al. in order to change cell surface receptor specificity of the native adenovirus to more efficiently target more clinically relevant target tissues. One of ordinary skill in the art at the time the invention was made would have had a reasonable expectation in producing the claimed invention because Stevenson et al. demonstrates that the chimeric adenovirus was able to transduce a panel of human cell lines, which include human airway cells and FaDu cells, indicating that certain tumor cells will be more effectively transduced with the new chimeric adenovirus than unfused Ad3/Ad5 recombinant adenoviruses used in the past. Therefore, the teachings of the art at the time the invention was made renders claims 1-4, 6-17, 20-23, 41, 47, and 69 obvious to one skilled in the art at the time the invention was made, absent unexpected results.

Claim 70 is rejected under 35 U.S.C. 103(a) as being unpatentable over Memerow et al. and Stevenson et al. as applied to claims 1-4, 6-17, 20-23, 41, 47, and 69 above, and further in view of Guo et al.

The claim is drawn to incorporating a tumor-suppressor gene into the recombinant adenovirus, taught by Memerow et al.

Guo et al. teaches a recombinant adenovirus expressing wild type p53. One of ordinary skill in the art at the time the invention was made would have been motivated to incorporate the tumor suppressor gene taught by Guo et al. in order to treat tumors or regress the growth of the tumor with the adenovirus taught by Memerow et al. and Stevenson et al. One of ordinary skill in the art would have had a reasonable expectation in producing the claimed invention because

Memerow et al. teaches that the recombinant adenovirus reduces risk of wild-type virus contamination, Stevenson et al. teaches that the transduction of human cells with a recombinant adenovirus increases with a chimeric fiber/tail and Guo et al. teaches success in reducing the growth rate of a recombinant adenovirus expressing the p53 gene. Therefore, in view of the teachings of the references, the invention as a whole would have been prima facie obvious to one skilled in the art at the time the invention was made.

Allowable Subject Matter

Claim 5, 18, and 19 are objected to as being dependent upon a rejected base claim, but would be allowable if rewritten in independent form including all of the limitations of the base claim and any intervening claims. The prior art does not teach or suggest the plasmids listed in claim 18, or SEQ ID NOs: 32, 43, 44, and 47.

Conclusion

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Shanon A. Foley whose telephone number is (703) 308-3983. The examiner can normally be reached on 7:30-4:30 M-F.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, James Housel can be reached on (703) 308-4027. The fax phone numbers for the organization where this application or proceeding is assigned are (703) 308-4242 for regular communications and (703) 308-4426 for After Final communications.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is (703) 308-0196.

Shanon Foley
June 15, 2001

MARY E. MOSHER
PRIMARY EXAMINER
GROUP ~~1700~~ 1600